

Amendments to the Specification:

Please replace the paragraph beginning at page 3, line 15, with the following rewritten paragraph:

-- Figure 1 represents the elution profile of the recombinant polypeptide with the amino acid sequence of SEQ ID NO:9 ~~SEQ ID No 9~~ purified by Superdex-200 chromatography, either before or after electron on NI-NTA. --

Please replace the paragraph beginning at page 3, line 25, with the following rewritten paragraph:

-- Figure 4 illustrates the flashplate time course of [³H]gabapentin binding to various concentrations of the recombinant polypeptide with the amino acid sequence of SEQ ID NO:9 ~~SEQ ID No 9~~. --

Please replace the paragraph beginning at page 7, line 15, with the following rewritten paragraph:

-- Figure 5 illustrates the capacity of the recombinant polypeptide with the amino acid sequence of SEQ ID NO:9 ~~SEQ ID No 9~~ in a flashplate assay after 3 hours of incubation.--

Please replace the paragraph beginning at page 4, line 1, with the following rewritten paragraph:

-- Figure 6 illustrates the optimum imidazole concentration, assayed after 3 hours of incubation, required to maximize [³H]gabapentin binding using a constant amount of the recombinant polypeptide with the amino acid sequence of SEQ ID NO:9 ~~SEQ ID No 9~~. --

Please replace the paragraph beginning at page 4, line 5, with the following rewritten paragraph:

-- Figure 7 illustrates flashplate assay of [³H]gabapentin saturation binding to the purified recombinant polypeptide with the amino acid sequence of SEQ ID NO:9 ~~SEQ ID No 9~~, assayed after 3 hours of incubation. --

Please replace the paragraph beginning at page 4, line 8, with the following rewritten paragraph:

-- Figure 8 illustrates the flashplate time course optimization of imidazole concentration required to maximize the [³H]Leucine binding window to the purified recombinant polypeptide with the amino acid sequence of SEQ ID NO:9 ~~SEQ ID No 9~~, assayed after 3 hours of incubation. --

Please replace the paragraph beginning at page 6, line 8, with the following rewritten paragraph:

-- The invention therefore particularly concerns a screening assay in which the secreted soluble $\alpha_2\delta$ -1 subunit polypeptide is preferably a polypeptide having at least 80% identity with the polypeptide comprising from amino-acid 1 to between amino-acid 985 and 1054, preferably between amino-acids 985 and 1059, and most preferably between amino-acids 1019 and 1064 of SEQ ID NO:5 or SEQ ID NO:16. Preferred $\alpha_2\delta$ -1 subunit polypeptides which can be used in the present invention are those of SEQ ID NO:6, ~~SEQ ID N°6~~, 7, 8, 9, 13, 14 and 15, with the polypeptides of SEQ ID NO:9 or SEQ ID NO:15 being most preferred. --

Please replace the paragraph beginning at page 7, line 14, with the following rewritten paragraph:

-- The most preferred embodiment contemplated by the inventors concerns the use of a purified tagged $\alpha_2\delta$ -1 subunit polypeptide. A particularly preferred tag is a nucleotide sequence encoding from 2 to 10, and preferably 6 histidine residues as provided in the polypeptide of SEQ ID NO:9 ~~SEQ ID No 9~~. --

Please replace the paragraph beginning at page 16, line 25, with the following rewritten paragraph:

-- The PCR products of Example 1 (3228bp JB189/JB195 derived PCR product coding for 6His tagged porcine $\alpha_2\delta$ -1b: SEQ ID NO:9 ~~SEQ ID No 9~~) were cloned into *Stu* I digested, calf intestinal phosphatase dephosphorylated, phenol chloroform extracted and

QIAEX gel purified pFastBac1 (Life Technologies) using the Rapid DNA ligation kit (Roche Diagnostics) transforming XL1-blue ($\alpha_2\delta$ -1b) *E. Coli* cells: --

Please replace the line beginning at page 17, line 8, with the following rewritten line:

-- SEQ ID NO:9 ~~SEQ ID No 9~~ in pFastBac1 --

Please replace the paragraph beginning at page 17, line 21, with the following rewritten paragraph:

-- Sequencing of pFBac-Porcine-s- $\alpha_2\delta$ -1- Δ 1040-1067-6His confirmed that the insert sequence corresponded to the nucleic acid encoding the polypeptide of SEQ ID NO:9, ~~SEQ ID No 9~~ except for the deletion of two bases from the 5' end of the 5' PCR primer (JB189). The loss of these two bases did not have any impact on the 5' end of the gene as the KOZAK translation start-site consensus (GCCACC) starts immediately after this deletion. --

Please replace the paragraph beginning at page 18, line 3, with the following rewritten paragraph:

-- One ng (5 μ l) of the recombinant pFastBac-1 construct containing the nucleotide sequence encoding the porcine $\alpha_2\delta$ -1 deletion mutant of SEQ ID NO:9 ~~SEQ ID No 9~~ was added to 100 μ l of DH10Bac cells thawed on ice. The cells were then mixed gently by tapping the tube then incubated on ice for 30 minutes before heat shock treatment by incubation in a 42°C water bath for 45 seconds. The mixture was then chilled on ice for 2 minutes before the addition of 900 μ l of S.O.C. medium. The mixture was then placed in a shaking incubator (200rpm) at 37°C for 4 hours. The cells were then serially diluted (10 fold dilutions from 10⁻¹ to 10⁻³) and 10 μ l of each dilution plated on LB agar plates containing 50 μ g/ml gentamicin, 10 μ g/ml tetracycline, 100 μ l/ml Bluo-gal and 40 μ g/ml IPTG. The plates were incubated at 37°C for between 1 and 3 days until discrete colonies of blue and white colour were discernible. --

Please replace the paragraph beginning at page 20, line 22, to page 21, lines 1-2, with the following rewritten paragraph:

-- The eluate was then loaded onto a Ni-NTA (Qiagen) column (2.5cm i.d. x 6cm h.) pre-equilibrated in 20mM Tris pH8.0, 0.5M KCl, 10mM Imidazole at a flow rate of 2 mg/min. The column was washed successively with buffer A (20mM Tris pH8.0, 0.5M KCl, 20mM Imidazole), buffer B (100mM Tris-HCl pH8.0, 1M KCl), and buffer A again. Elution was performed with buffer C (20mM Tris-HCl pH8.0, 100mM KCl, 0.5M Imidazole). The Ni-NTA eluate (~50ml) was concentrated (30kDa cut-off) to ~2ml and applied at 1ml/min and in 0.2ml aliquots, to an FPLC Superdex-200 column equilibrated in 10mM HEPES, pH7.4, 150mM NaCl. Fractions containing the polypeptide of SEQ ID NO:9 ~~SEQ ID No 9~~ were pooled. As shown in Figure 1, the protein elution profile and associated [³H]gabapentin binding activity is presented together with a silver-stained SDS-PAGE gel (post Ni NTA load of Superdex-200) demonstrating the co-elution of the ~130kDa band ($\alpha_2\delta$) with the [³H]gabapentin binding activity and A_{280nm} profile. --

Please replace the paragraph beginning at page 21, line 6, with the following rewritten paragraph:

-- The assay was carried out at 20°C. Assay components were added in the following order (all reagents were diluted in 10mM HEPES (pH 7.4 at 21°C) to 96-well Optiplates:

25μl imidazole at various concentrations (diluted from a 1M stock pH8.0, see assay details)

50μl 10mM HEPES pH 7.4

25μl (50mg) SPA beads (Amersham)

100μl s- $\alpha_2\delta$ -1b-6His of SEQ ID NO:9 ~~SEQ ID No 9~~ (2μl protein diluted to 100μl) obtained from example 5 --

Please replace the paragraph heading beginning at page 21, line 26, with the following rewritten paragraph heading:

-- Ni Flashplate assay of [³H]gabapentin binding to soluble porcine $\alpha_2\delta$ -1b-6His (SEQ ID NO:9) (SEQ ID No 9) --

Please replace the paragraph heading beginning at page 24, line 10, with the following rewritten paragraph heading:

-- **Ni Flashplate assay studying competitive binding of [³H]gabapentin, (S+)-3-isobutyl GABA and (R)-3-isobutyl GABA to porcine $\alpha_2\delta$ -1b-6His (SEQ ID NO:9) (SEQ ID No 9) --**

Please replace the paragraph heading beginning at page 26, line 6, with the following rewritten paragraph heading:

-- **Filter binding assay of [³H]gabapentin binding to the recombinant polypeptide of SEQ ID NO:9 SEQ ID No 9 --**

Please replace the paragraph beginning at page 26, line 9, with the following rewritten paragraph:

-- Assays were carried out at 21°C in a final volume of 250µl in 96-deep well plates.

Assay components were (all reagents were diluted in 10mM HEPES (pH 7.4 at 21°C)):

25µl compound to test

200µl Polypeptide of SEQ ID NO:9 ~~SEQ ID No 9~~ (3µl protein diluted to 200µl)

25µl radioligand ([³H]gabapentin (65Ci/mmole) --